

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendments, claims 29-30, 32-33, 78-79 and 82-125 are pending in the application, with 29, 33 and 78 being the independent claims. Claims 1-28, 31, 34-77 and 80-81 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. These changes are believed to introduce no new matter, and their entry is respectfully requested. Support for amendments to the claims can be found in the claims as originally found. Additionally, support for "wherein said antibody does not inhibit tissue factor mediated blood coagulation compared to a normal plasma control and causes an increase in percent cytotoxicity of tissue factor positive cells compared to a negative control antibody" can be found, for example, at page 79, paragraph 205 and in Figures 4A-4C. Support for "wherein said antibody is administered to the subject at a dosage of 0.001 mg/kg to 100 mg/kg of the subject's body weight" can be found, for example, at page 62, paragraphs 169-170. Support for new claims 82-125 can be found, for example, in the original claims as filed. Specifically, support for claims 82-88, 97-103 and 110-116 can be found, for example, in original claims 4 and 5. Support for claims 89-90, 104 and 117 can be found, for example, in original claims 8 and 9. Support for claims 91-95, 105-109 and 118-122 can be found, for example, in original claims 14, 15, 20, 21, 36, 37 and 39 and in the specification at page 6, paragraph 26 and page 7, paragraphs 28 and 30. Support for claims 96 and 123 can be found, for example, in original claim 7. Support for claims 124-125 can be found, for example, in original claim 28.

Based on the above amendments and the following remarks, Applicant respectfully requests that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Restriction Requirement

Applicant acknowledges that the Examiner has deemed the Restriction Requirement final.

Interview Summary of Mail Date August 1, 2007

In reply to the Interview Summary Form PTOL-413 mailed August 1, 2007, and in accordance with 37 C.F.R. § 1.133(b) and MPEP § 713.04, Applicant's undersigned representative provides the following statement of the substance of the interview held with the Examiner in the above-captioned application.

The Examiner, Applicant's undersigned representative and Judith Kim participated in a telephonic interview on July 26, 2007. Applicant agrees with the statements regarding the July 26, 2007 interview in the Examiner's Interview Summary. Claims 29-34 and 78-90 were discussed in the July 26, 2007 interview along with the reference Edgington *et al.*, which was cited in the April 6, 2007 Office Action. Each of the rejections in the Office Action was discussed. The claim amendments and arguments made in this Amendment and Reply were also discussed in the July 26, 2007 interview. The Examiner requested that Applicant's arguments be submitted in this Amendment and Reply for his consideration. Although agreement was not reached, Applicant's representatives found the interview helpful. Applicant and Applicant's representative

thank the Examiner for taking time from his busy schedule to hold the telephonic interview.

Rejections Under 35 U.S.C. § 112

Claims 29, 30, 32, 33, 78 and 79 were rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for methods of diagnosing non-small cell lung, breast, colon and prostate cancer by administering antibodies that bind tissue factor but do not inhibit tissue factor mediated coagulation, and being enabled for methods of treating lung and breast cancer by administering said antibodies, allegedly does not reasonably provide enablement for methods of treating and diagnosing the genus of all cancers using the antibodies of the present invention.

Solely to advance prosecution and not in acquiescence to the Examiner's rejection, Applicant has amended independent claims 29, 33 and 78 to recite "wherein said cancer is selected from the group consisting of non-small cell lung cancer, breast cancer, colon cancer and prostate cancer." The remaining pending claims are dependent claims. Applicant respectfully requests this rejection be withdrawn.

Rejections Under 35 U.S.C. § 102

Claims 29-34 and 78-80 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Edgington *et al.*, U.S. Patent No. 5,223,427. Applicant respectfully traverses.

In the Office Action at page 7, the Examiner alleged that Edgington *et al.* teaches an antibody that does not inhibit tissue mediated blood coagulation as well as methods of

using this antibody to treat breast and lung cancer when the antibodies are coupled to an anti-tumor agent and administered as part of an anti-tumor therapeutic composition and methods of detecting the antibody.

In contrast, amended independent claims 29, 33 and 78 recite administering an antibody that "does not inhibit tissue factor mediated blood coagulation compared to a normal plasma control *and* causes an increase in percent cytotoxicity of tissue factor positive cells compared to a negative control antibody, wherein the antibody is administered to the patient at a dosage of 0.001 mg/kg to 100 mg/kg of the patient's body weight" Emphasis added.

To qualify as prior art under 35 U.S.C. § 102(b), a reference must teach each and every element of a claim. *See* MPEP 2131 (citing *Verdegaal Brothers v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987)).

Edgington *et al.* does not teach or disclose an antibody that (1) does not inhibit tissue factor mediated blood coagulation *and* (2) causes an increase in percent cytotoxicity of tissue factor positive cells compared to a negative control antibody. Furthermore, Edgington *et al.* does not disclose administering the antibody to the patient at a dosage of 0.001 mg/kg to 100 mg/kg of the patient's body weight. Thus, Edgington *et al.* does not anticipate the pending claims and the rejection under 35 U.S.C. § 102(b) should be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 29, 31, 33, 34, 78 and 80 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Edgington *et al.* in view of Koomagi *et al.* As

explained above, the Examiner alleged that Edgington *et al.* teaches an antibody that does not inhibit tissue mediated blood coagulation as well as methods of using this antibody to treat breast and lung cancer and methods of detecting the antibody. Additionally, the Examiner alleged that Koomagi *et al.* teaches, *inter alia*, that tissue factor expression has predicative value in estimating survival for patients with non-small-cell lung cancer. *See* Office Action, p. 8. Applicant respectfully traverses.

As discussed above, amended independent claims 29, 33 and 78 recite administering an antibody that "does not inhibit tissue factor mediated blood coagulation compared to a normal plasma control and causes an increase in percent cytotoxicity of tissue factor positive cells compared to a negative control antibody, wherein the antibody is administered to the patient at a dosage of 0.001 mg/kg to 100 mg/kg of the patient's body weight"

To establish a *prima facie* case of obviousness, the art cited by the Examiner must (1) teach all of the claim limitations; (2) provide a suggestion or motivation to those of ordinary skill in the art to make the claimed composition; and (3) reveal that one of ordinary skill would have a reasonable expectation of success in doing so. *See In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); *see also* M.P.E.P. § 706.02(j). The Supreme Court, in *KSR International vs. Teleflex, Inc.*, 127 S.Ct. 1727 (2007), further clarified the requirements for obviousness analysis under 35 U.S.C. § 103(a). The Court noted that the analysis supporting a rejection under 35 U.S.C. § 103(a) should be made *explicit*, and that it was "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements" in the manner claimed. The Court specifically stated:

[o]ften, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was ***an apparent reason*** to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, ***this analysis should be made explicit***. KSR at 1742, citing *In Re Kahn*, 441 F. 3d 977,988 (CA, Fed. 2006) ([R]ejections on obviousness grounds ***cannot be sustained by mere conclusory*** statements, instead, there must be some articulated reasoning with some rational underpinning to support a legal conclusion of obviousness.").

According to Edgington *et al.*, huTFh factor VII/VIIa binding site polypeptide analogs and *anticoagulant* MoAbs can be used to modulate the binding of factor VII/VIIa by tissue factor in vivo. Col. 22, ll. 37-41. This is supported by Table 8 (cols. 50-51), which shows that 23 MoAbs that inhibited TF activity also blocked factor VII/VIIa binding but, as expected, the MoAb that did not inhibit TF activity, TF9-10H10 (a "non-neutralizing MoAb"), did not block factor VII binding (col. 53, ll. 3-7). Edgington *et al.* also disclose that "the antibody molecules of a MoAb, anticoagulant MoAb or non-neutralizing MoAb of the present invention are linked to an anti-tumor agent to form an anti-tumor therapeutic composition." Col. 23, ll. 3-11. However, Edgington *et al.* do not teach or suggest an antibody that (1) does not inhibit TF activity *and* (2) can itself cause an increase in percent cytotoxicity of tissue factor positive cells, as recited in the presently claimed invention. At most, Edgington *et al.* suggest to use TF9-10H10 to detect a thrombus (col. 26) or for targeting an anti-tumor agent to tumor cells that express TF (col. 23), i.e., as a carrier for delivering an anti-tumor agent to tumor cells that express TF. Koomagi *et al.* fail to remedy the deficiencies of Edgington *et al.*

Although the pending claims encompass conjugating the antibody of the present invention to a cytotoxic agent, the Examiner is legally required to consider the claimed

invention as a whole, and the combination of Edgington *et al.* and Koomagi *et al.* fails to teach or suggest an antibody that (1) does not inhibit tissue factor mediated blood coagulation *and* (2) causes an increase in percent cytotoxicity of tissue factor positive cells compared to a negative control antibody, as recited in the present claims. Moreover, based on Edgington *et al.* and Koomagi *et al.*, one of ordinary skill in the art would have had no reasonable expectation of successfully making an antibody that does not inhibit tissue factor mediated blood coagulation and that causes an increase in percent cytotoxicity of tissue factor positive cells compared to a negative control antibody, as recited in the present claims. The antibody of the claimed invention, having the recited features, was not contemplated by Edgington *et al.* or Koomagi *et al.* Applicant respectfully requests the rejection under 35 U.S.C. § 103(b) over Edgington *et al.* in view of Koomagi *et al.* be withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Amdt. dated August 6, 2007
Reply to Office Action of April 6, 2007

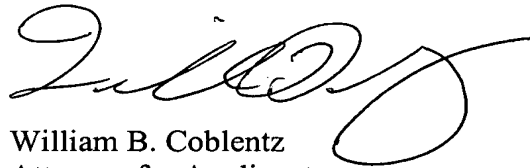
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Prompt and favorable consideration of this Amendment and Reply is respectfully
requested.

Respectfully submitted,

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